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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/995,335	11/27/2001	Antonio Verdini	29964/ 37956	9651

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EXAMINER	
LUKTON, DAVID	
ART UNIT	**PAPER NUMBER**
1653	

DATE MAILED: 01/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/995,335	VERDINI ET AL.	
	Examiner	Art Unit	
	David Lukton	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 December 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-27* is/are pending in the application.

4a) Of the above claim(s) *13-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicants' election of Group I (claims 1 and 3-12) is acknowledged. Also acknowledged are the species:

(a) the specific polypeptide which is to be folded is hu-I-309, as described in example 4, pages 15-16;

(b) the specific "chaotropic salt" is guanidinium chloride;

(c) the pH at which the folding is to take place is 8.0.

(d) cysteine is the reducing agent that is present in the folding buffer

Claims 13-27 are withdrawn from consideration.

✧

Claims 1 and 3-12 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- Claim 1 recites the following:

  "A process for folding ... polypeptides comprising treating a polypeptide and/or protein ... with a reducing agent..."

  Thus, applicants have drawn a distinction between proteins and polypeptides. The skilled artisan would recognize that there is considerable overlap between the meaning of the term "protein" and the meaning of the term "polypeptide". But given that applicants have used both terms in the claim, it appears that applicants intend for there to be some sort of distinction between them. The nature of that distinction is not

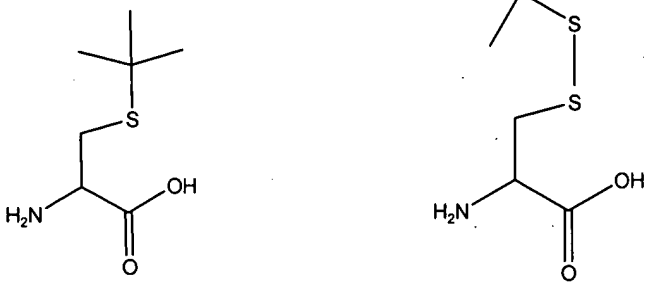
made clear, however. In particular, the claim recites that one can treat a protein with a reducing agent, and wind up, not with a protein, but rather, with a polypeptide. How is it that applicants are able to take a protein, and transform it into a polypeptide...? A related issue concerns the presence of the term "and" within the following phrase:

"comprising treating a polypeptide **and**/or protein".

Thus, the claim recites in effect that one can take a mixture of a "first compound" and a "second compound", treat it with a reducing agent, and wind up with a polypeptide, wherein the "first compound" is a polypeptide, and the "second compound" is a protein. However, it is unclear how this transformation is to be achieved.

- In claim 1, second-to-last line, the term "residue" is used in the singular. The recitation of the term "residue" is present within the phrase "the derivatized cysteine residue". Accordingly, the phrase at issue ("the derivatized cysteine residue") can be said to lack antecedent basis. It is true that the phrase "two or more derivatized cysteine residues" is present earlier in the claim, but recitation of the term "residue" in the singular, in conjunction with the definite article ("the") raises a question about which of the various cysteines is being referred to. One option would be to recite that <u>each</u> of the derivatized cysteine residues is S-*tert*-butyl-thiocysteine. Alternatively, the claim might specify that at least one of the derivatized cysteine residues is S-*tert*-butylthiocysteine, or at least two, etc.

- Claim 1 makes reference to "S-butyl-thio-cysteine". The first point is that the term "butyl" encompasses four different isomers. If there is descriptive support for it, applicants can modify the claim to make it clear that inclusion of all three isomers is intended. (No determination has been made by the examiner as to what would, or would not constitute new matter). But suppose, for purposes of discussion, that the *tert*-butyl isomer is intended. the next issue pertains to the fact that even if the *tert*-butyl isomer were specified, the claim would still be unclear as to the intended derivative. Given the name that is provided, either of the following could potentially be intended:



As it happens, both of these are known. For example, Felix (*International Journal of Peptide and Protein Research* **11**(5), 329-339, 1978) discloses the first of these two possibilities. The second of these is a mixed disulfide, and is also known in the prior art. The claims, or at least the specification, should make clear which of these is intended.

- Claim 1 recites that the derivatized cysteine residue "corresponds to" S-butyl-thio-cysteine. What is meant by "corresponds to"...? Does this mean that the derivatized cysteine residue **is** S-butyl-thio-cysteine...?

✧

The following is a quotation of 35 USC. §103 which forms the basis for all obviousness rejections set forth in the Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made, absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103.

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Birr, C. (*Angew Chem. Int. Ed. Engl.* 18, 147-148, 1979)

Birr discloses (Scheme 2) preparation of a peptide containing two cysteines, in which each of the two cysteines is protected with a *tert*-butylmercapto group. Also shown is that the *tert*-butylmercapto groups were removed by treating the peptide with triphenylphosphine under nitrogen. Subsequent exposure to oxygen led to production of a disulfide bond. Birr does not disclose that the tertiary structure of the peptide containing the disulfide bond is different from that of the peptide containing no disulfide bonds. However, the peptide chemist of ordinary skill would regard it as inevitable that the conformation of any peptide will undergo a dramatic change on cyclization, whether that cyclization occurs by formation of disulfide bonds, or "head to tail" bond formation or Lys/Glu side chain bonding (or any other means of cyclization). That change in conformation is a "folding" of sorts.

Thus, the claim is rendered obvious.

✧

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Moroder

(*Biopolymers* **20**, 17-37, 1981).

Moroder discloses (Scheme 1, page 30) preparation of somatostin (A-G-C-N-F-F-W-K-T-F-T-S-C), which contains two cysteines. Each of the two cysteines was protected with a *tert*-butylmercapto group. Also shown is that the *tert*-butylmercapto groups were removed by treating the peptide with triphenylphosphine. Subsequent exposure to oxygen led to production of a disulfide bond. Moroder does not disclose that the tertiary structure of the peptide containing the disulfide bond is different from that of the peptide containing no disulfide bonds. However, the peptide chemist of ordinary skill would have expected a significant change in the amount of "folding" between an acyclic peptide containing two cysteines, and the corresponding cyclic peptide in which the sulfhydryl groups are bonded together.

Thus, the claim is rendered obvious.

✧

Claim 1 is rejected under 35 U.S.C. §103 as being unpatentable over Birr (USP 4,351,764).

Birr discloses (fig. 4) preparation of a peptide containing two cysteines, in which each of the two cysteines is protected with a *tert*-butylmercapto group. Also shown is that the *tert*-butylmercapto groups were removed by treating the peptide with triphenylphosphine. (See also col 5, line 65 and col 7, line 41). Subsequent exposure to oxygen led to

production of a disulfide bond. Birr does not disclose that the tertiary structure of the peptide containing the disulfide bond is different from that of the peptide containing no disulfide bonds. However, the peptide chemist of ordinary skill would recognize that the "folding" of the disulfide-bonded peptide will be different from the "folding" of the linear peptide.

Thus, the claim is rendered obvious.

✹

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Lukton whose telephone number is 571-272-0952. The examiner can normally be reached Monday-Friday from 9:30 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber, can be reached at 571-272-0925. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.

D. Lukton

DAVID LUKTON
PATENT EXAMINER
GROUP 1653